REMARKS

In the Office Action of March 19, 2004, claims 11-13 were rejected under 102(a) in view of Yang et al., and claims 15-17 were objected to as depending on a rejected claim.

In response to the rejection of claims 11-13, we enclose the Declaration Under 37 C.F.R. 1.131 of Theodore E. Spielberg affirming that he made the invention defined by these claims prior to January 1, 1994, i.e., prior to the asserted date of the Yang reference.

In response to the objection to claims 15-17, we have amended claim 17 to remove reference to a non-elected claim (claim 1). In light of the attached Declaration, claims 11-13 should now be allowable, and thus claims 15-17 as well.

Please charge any additional fee occasioned by this paper to our Deposit Account No. 03-1237.

Respectfully submitted,

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Claims 11-13DECLARATION UNDER 37 C.F.R. §1.131 OF THEODORE E. SPIELBERG

Theodore E. Spielberg, on the basis of personal knowledge, declares as follows:

1. I am the inventor of the subject matter of the above patent application.

2. I am advised that claims 11-13 of the above application have been rejected on the basis of an article "Comparative studies of in vitro and in vivo function of three different bioartifical pancreases made of agarose hydrogel" by Yang et al., Biomaterials 1994, vol. 15, No. 2, January 1994.

As set forth in detail herein, I conceived of the subject matter of these claims within the United States prior to January 1, 1994 and was diligent in reducing it to practice in the United States since the time of conception by filing an application thereon.

3. In particular, the attached "Exhibit A" is a true copy of a portion of notes that I made in connection with documenting the invention. These notes are in my own handwriting, and were made prior to January 1, 1994. A transcription of a portion of the notes specifically discussing the endocrine cell microdisk as defined by claims 11-13, among others, is attached as Exhibit B.

I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true, and further that these statements were made with the knowledge that willful false statements and the like are punishable by fine or imprisonment or both under 18 U.S. Code §1001 and that any

such willful false statement may jeopardize the validity of the application or any patent issued thereon.

May 31, 2005
Date

Theodore E. Spielberg, M.D.

Exhibit A

Brief Description of the Invention:

Instead of the spherical shape of current microcapsules the endocrine cell containing microcapsules are generally flattened on two sides creating coin or pill shapped or microdisks microcapsules. This effectively increases the surface/volume ratio of the devices and increasing their diffusional capacity per unit of time. Moreover, when transplanted in a body cavity with large surfaces (vascular membranes) such as the peritoneal cavity they align themselves along these surfaces on one of their flat sides, increasing the surface area of the device in contact with the vascular surface and reducing the diffusion distance. This further enhances the diffusion rate of oxygen and carbon dioxide as well as nutrients and glucose and insulin between the host and the microdisk resulting in increased efficiency as well as increased support of the enclosed transplanted endocrine cell. Even though the microdisk enclosed flat on two sides resulting [illegible] as a result of endocrine cell [illegible] may exist a mild convexity in a discoid or pill-like appearance. Thus, the endocrine cell microdisk achieves increased efficiency and support intrinsically on the basis of its favorable geometry with increased surface/volume ratio as well as its enhanced interaction with vascular body surfaces as a result of its increased contact area. Additionally, when in smaller body cavities, such as the renal capsule, the endocrine cell microdisks can be stacked allowing more endocrine cells per unit area than could be achieved with microspheres. This allows the transplantation of more endocrine cells at a given body site and delivering more [illegible] and may obviate the need for utilization of multiple sites and [illegible] surgical procedures.

Diffusion rate of a substance = Concentration X Cross sectional surface area [illegible] of [illegible]

In a preferred embodiment the endocrine cell microdisk is further enhanced by central dimpling of one or both of its flattened surfaces creating an endocrine cell biconcaval microdisk. This uniconcaval or biconcaval microdisk further increases the surface/volume ratio of the device while preserving its stacking ability.

Comparing an endocrine cell microsphere with an endocrine cell biconcave microdisks of the same total volume of 90 μm^3, the surface area of the microsphere is 98 μm^2, while the surface area of the concave microdisk is 140 μm^2.

Detailed Description of the Invention

Since the main application of this device is as an artificial endocrine pancreas for the treatment of Diabetes mellitus, an insulin producing islet cell microdisk or uniconcaval or biconcaval microdisk will be described.

Insulin producing islet cells (beta cells) are separated from the exocrine pancreas by Collagenase digestion and purified by density gradient centrifugation as is well-known in the art. These cells are combined with various substances to produce microporous microspheres encapsulating them. Some substances well-known in the micro-encapsulating art are alginate, barium alginate, alginate polylysine alginate, alginate-polylysine-alginate, agarose, agarose-polystyrene, Hydrogels and polyion complexes, and polymers such as hydroxy-ethyl/methacrylate-methyl/methacrylate (HEMA-MMA), and AN69 (Polyacrylonitrile).

Exhibit B

Brief Description of The Invention.

Instead of the spherical shape of current microcapsules the endocrine cell containing microcapsules are generally flattened on two sides creating coin or pill shaped microcapsules or microdisks. This effectively increases the surface/volume ratio of the devices and increases the diffusional capacity per unit of time.

Moreover, when transplanted in a body cavity with large surfaces (vascular membranes) such as the peritoneal cavity they align themselves along these surfaces on one of their flat sides, increasing the surface area of the device in contact with the vascular surface and reducing the diffusion distance. This further increases the diffusion rate of oxygen and carbon dioxide as well as nutrients and glucose and insulin between the host and the microdisk resulting in increased efficiency as well as increased support of the enclosed transplanted endocrine cell.